THE TREATMENT OF INFECTIVE DISEASES BY BACTERIAL VACCINES.

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BY

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THE TREATMENT OF INFECTIVE DISEASES BY BACTERIAL VACCINES.

Mr. President and Gentlemen,

When your Secretary, Dr. Broadbent, invited me to read a paper on the treatment of infective diseases by bacterial vaccines, an honour which I appreciate highly, I hoped to keep Professor Osler's advice to medical societies in view and keep it short. I find, however, that the subject is very difficult to abbreviate.

First we have to be clear as to the exact nature of the remedy we are applying.

Secondly, we need knowledge of its mode of action.

Lastly, to know the procedure that should guide dosage, and the results of our experience in treatment.

1. A bacterial vaccine consists simply of an emulsion of sterilised bacteria of known numbers per volume.

In the past they have been prepared in many ways, but now the procedure is as follows :—

Preparation of vaccine.—The organism is grown in pure culture in a nutrient medium for twenty-four hours at blood heat. It is then removed and emulsified by rubbing it up with saline sol. (0.1%) in an agate mortar. After this it is centrifuged and washed, but no attempt is made to triturate or treat it otherwise than by mixing well. It is now standardised, that is, the numbers per c.c. are counted approximately. A sufficient volume is pipetted off containing the desired number of bacteria for a dose. This is sterilised and sealed in a vial ready for use by subcutaneous injection with aseptic precautions.

While this method is adopted for staphylococcus, streptococcus, pneumococcus, colon, etc., vaccines, the new tuberculin T.R. is tritrated more vigorously and disintegrated, then centrifuged and filtered, and is a solution of the bacilli. It contains 2 mgm. solid to 1 c.c.

2. *Mode of action of vaccine.*—I come now to the mode of action of vaccines as far as is known. This really introduces the subject of immunity, or the method by which the body protects itself against infection with the result that the bacteria are held in check or disposed of. Immunity is itself described as spontaneous or acquired.

Spontaneous immunity.—Spontaneous immunity is seen in races in the comparative insusceptibility of the black man to yellow fever and malaria while the susceptibility of the Pacific Islanders to measles is known. Again, Algerian

sheep and white rats are insusceptible to anthrax, while European sheep and the brown rat are highly susceptible.

Acquired immunity.—Acquired immunity, on the other hand, results either as the natural sequence of infective disease and is well seen after small-pox, scarlet and yellow fevers, or as a transient state after diphtheria, pneumonia or erysipelas, or as the results of treatment.

Active (a).—Immunity is produced in two ways, either actively or passively: active immunity by seeking to call into action the natural protective processes of the body. An example is seen in vaccinia where vaccination is practised and the mild resulting infection protects against variola. Similarly, but by artificial means, the defensive mechanism is put in play by the administration of bacterial vaccines which produce anti-bodies.

Passive (b).—For various reasons vaccination is the fashion just now and is receiving an extensive trial, but I would emphasise that immunity can also be produced *passively*. This results from the introduction into the body of anti-bacterial or anti-toxic substances or sera, obtained *ready made*, so to speak, from animals, by the process of inoculating them either with bacteria or bacterial toxins.

The most favourable example of this is seen in diphtheria in which the mortality has been reduced from 29.29 per cent. of patients treated in 1894 to 11.15 in 1901 (Metropolitan Asylums' Board). In Chicago the five years pre anti-toxin period exceeded by 42 per cent. the actual number of deaths in the succeeding five years.

The question arises, "Why not use sera more frequently?"

The reason is that a serum of high potency cannot always be produced. I will attempt a possible explanation.

Diphtheria and tetanus differ from most infective diseases as tubercle, staphylococcus, streptococcus, pneumococcus, plague, Malta fever, etc., in being "intoxication" diseases, and their germs, when grown in broth, produce soluble poisons or toxins. Staphylococci, etc., produce little or no *soluble* toxins. We have seen that it is from the injection of these toxins into animals that the production of protective (and curative) substances or anti-toxic sera result. Thus the injection of sterile cultures of certain infective bacteria results in little or no anti-toxin being formed, though anti-bacterial bodies may be.

In short, the injection of bacteria or their toxins in animals does not always result in a *proportionate* amount of these anti-toxins being formed. Hence there is no cumulative action in inoculation, sera of a high potency cannot always be obtained, and lack of success has resulted in their use. The reason for the extreme potency of diphtheria anti-toxin I cannot explain.

I mention some of the substances which may be present in the blood and which are hostile to the presence of bacteria.

Bactericidal bodies kill bacteria, bacteriolysins dissolve them, agglutinins and precipitins compel bacteria to clump together, opsonins help to prepare bacteria for digestion, etc.

Some of these bodies are complex, being composed of two substances. Thus bacteriolysis depends on the presence of two substances. One is specific, that is specially antagonistic to the microbe in question (and can be formed by inoculating an animal with the microbe); the other substance is present in ordinary blood serum and rapidly disappears if blood is drawn.

The former is known as "immune body" (amboceptor) and being able to withstand heating to 60° C. is called thermostable. The latter is known as complement (receptor, alexin, addiment, cytase or hapton) and is thermolabile.

As these opsonins prepare bacteria for ingestion by leucocytes much importance is attached to their study, but I am equally sure that the study of phagocytosis cannot be neglected.

Phagocytosis or the ingestion of foreign bodies by leucocytes is usefully distinguished as "spontaneous" and "induced." Spontaneous phagocytosis is defined as that process of ingestion which occurs when bacteria or inert particles which have not been acted upon by the blood fluids are submitted to the action of washed leucocytes in an indifferent medium (as physiological salt solution). It differs from that known as induced phagocytosis in certain respects, being less rapid and less complete. Induced phagocytosis is that observed when leucocytes are brought in contact with bacteria which are or have been submitted to the action of serum.

The experiments of Wright and Douglas go to prove that phagocytosis is very largely dependent upon the presence in the blood plasma and serum of these opsonic

substances, while the leucocytes are regarded as playing a subordinate part. As a corollary, immunity or cure, when brought about by vaccine treatment (which stimulates the formation of opsonins and raises the "opsonic content" of the blood) may be said to result from changes in the blood fluids rather than in the white corpuscles. On this depends the belief that the "opsonic index" of blood is the gauge of a person's powers of phagocytosis, because the person's own leucocytes are neglected as a factor, and indeed are not used in the experiment. Wright and Douglas believe that differences in the phagocytic count depend on the properties of the serum not on the "strain of the leucocytes, *æqualia æqualibus*."

In my opinion this distinction may be too rigidly drawn. Variations in structure and function are infinite in the animal body, and why should the blood cells escape them ?

Thus the powers of phagocytosis of the different varieties of leucocytes in the same person are well known to differ, and this I and Dr. Williams have demonstrated.

Again, at the Exeter meeting of the British Medical Association I described some observations made in the Ralli Laboratory, which showed that the polynuclear leucocytes of a healthy person were threefold as phagocytic as those of a patient with myelocythæmia, *æqualia æqualibus*. The variation from normal leucocytes in this case was therefore both of structure and function.

Also the brilliant work of Dr. Opie is quoted in Sir A. E. Wright's address in *The Lancet* of August (17th and 24th) last in this respect, in which Dr. Opie indicates that in addition to ingestion of bacteria by leucocytes, digestion must occur, if the patient is to be protected. Dr. Opie has proved that leucocytes, freed from blood serum, are able to digest blood clot and gelatine, though *not* in the presence of serum.

This reminds us of Metchnikoff's views of the importance of phagocytes and of their digestive ferments.

On these grounds the further study of the leucocytes is requisite and further points at once suggest themselves for research. Shattock and Dudgeon confirm this view, that immune leucocytes may have a higher phagocytic power than normal ones (April, 1908, Royal Soc. Med.)

A word as to our knowledge of opsonins. Muir and Martin (Proc. Roy. Soc. B. Vol. 79, 1907) believe them to be of two classes ; one of the nature of immune body

(specific substances) resistant to heat; the other of the nature of complement, an unstable substance in normal serum. Wright and Bulloch (*Lancet*, 1905; II, p. 1605) consider them to be specific; Simon (Jour. Eper. Med. Vol. VII., December 14th, 1906, No. 6) does not find them so. Dean (Proc. Royal Soc., Vol. I. and XVI.) and also Smith have shown that they are not altogether destroyed by heat, which agrees with Muir and Martin's work. (The opsonic power is said to stand at about half of what it was originally after standing five or six days. Simon considers that it is necessary to make dilutions of the serum to estimate the opsonic content.)

III. The last consideration is the administration of the vaccine, and this is all-important when we remember the disastrous effects that followed over dosage with Koch's old tuberculin. Therefore I quote to you the practice of Sir A. E. Wright:—

"Where an examination of the patient's blood taken twenty-four hours before inoculation shows a subnormal index and examination of his blood taken twenty-four hours after inoculation shows that the index has been considerably reduced, I take it that a smaller dose would have been appropriate. Where examination of the blood twenty-four hours after inoculation shows that the index has been raised, and where after the expiration of a week or ten days the index has fallen back to what it was before inoculation—I take it that a larger dose might appropriately have been administered. Where in association with a slight initial fall after inoculation, the index is after the expiration of a week or ten days found to stand higher than it was at the outset, I take it that an appropriate dose has been administered."

However, Simon and his co-workers claim that the opsonic content of a person's blood varies much more than the determination of the opsonic index by Wright's method shows. For an opsonic index to be a safe guide as I have indicated extreme technical care and expenditure of time is necessary. Thus the opsonic index is said to range in healthy persons (Wright and Bulloch) from 0.8 to 1.2 for tubercle. Now, if the serum of a patient be compared with that of an individual whose standard is 0.8 and his opsonic index were 0.9, he is said to be free from tuberculosis, whereas if the standard serum were 1.2 his index would be 0.6 or tuberculous.

At the Sussex County Hospital we have examined the opsonic index of about 100 patients, some a great number of times, and certain of these have been treated by vaccines and improved. These have been tuberculous, staphylococcal and streptococcal infections and we feel justified in saying that, in cases properly selected, good results have accompanied the administration of vaccines and ill effects can be avoided.

A happy medium is to be drawn between a too rosy and a too pessimistic view of the value of vaccine treatment.

Opsonic indices of some ninety cases examined at the Sussex County Hospital, up to September, 1907.

1—TUBERCULOSIS.

G. B. (M) *Tubercle of hip.*

10/ 1/6	0.8		15/ 3/6	0.3	
16/ 1/6	0.9		17/ 3/6	0.5	
18/ 1/6	0.8		22/ 3/6	1.08	
22/ 1/6	1.2		6/ 4/6	0.6	
23/ 1/6	1.2		9/ 4/6	1.3	
29/ 1/6	0.7		14/ 4/6	0.9	TR.
30/ 1/6	0.9		17/ 4/6	2.8	
1/ 2/6	0.9	TR. $\frac{1}{1000}$	23/ 4/6	0.99	TR. Good fixation of joint obtained.
7/ 2/6	0.5			0.2	
13/ 2/6	0.7		30/ 4/6	0.8	
26/ 2/6	1.3		2/ 5/6	1.3	
			7/ 5/6	1.3	

C. B. (F) *Anæmia.*

12/ 3/6 1.4

C. V. (F) *Tuberculous broncho-pneumonia, vomica, septicæmia, parotitis.*

14/ 5/6 1.1

G. A. (M) *Meningitis.*

12/ 3/7 1.0

H. S. (M) *Empyema.*

30/ 3/7 1.2
2/ 4/7 1.3
5/ 4/7 0.6
6/ 4/7 1.1

M. G. (F) *Abscess of Thigh.*

11/ 7/7 1.1

E. M. (F) *Myelocythæmia.*

25/ 7/7 1.4

D. C. (M) *Tubercle of Knee.*

22/ 4/7 1.4

K. L. (F) ————(?)

6/ 8/7 1.4

L. W. (F) *Phthisis.*

24/ 7/7 1.1

W. C. (M) 40. *Tubercle of femur.*

3/ 4/6	1.0	
11/ 4/6	0.9	
14/ 4/6	1.05	
17/ 4/6	2.8	
23/ 4/6	1.7	TR.
	2.0	
30/ 4/6	0.7	
2/ 5/6	? 0.17	
7/ 5/6	0.8	
8/ 5/6	1.3	
14/ 5/6	1.6	
15/ 5/6	0.9	
21/ 5/6	1.5	
22/ 5/6	1.2	
28/ 5/6	2.0	
29/ 5/6		TR. $\frac{1}{500}$ mgm.
30/ 5/6	0.9	
4/ 6/6	0.6	
7/ 6/6	1.5	
12/ 6/6	1.1	
18/ 6/6	1.3	
19/ 6/6		TR. $\frac{1}{500}$ mgm.
20/ 6/6		
21/ 6/6		TR. $\frac{1}{500}$ mgm.
25/ 6/6	1.2	
26/ 6/6		TR. $\frac{1}{500}$ mgm.
27/ 6/6	1.3	
3/ 7/6	0.8	
4/ 7/6		TR. $\frac{1}{500}$
9/ 7/6	1.0	
11/ 7/6		TR. $\frac{1}{500}$
17/ 7/6	0.9	TR. $\frac{1}{500}$
23/ 7/6	1.8	
24/ 7/6		TR. $\frac{1}{500}$
30/ 7/6	1.8	
31/ 7/6	1.3	TR. $\frac{1}{500}$
6/ 8/6	1.0	
7/ 8/6		TR. $\frac{1}{500}$
24/ 8/6	0.8	
6/ 9/6	0.6	
11/ 9/6	1.0	
17/ 9/6	1.3	
3/ 6/7	1.2	

Slow improvement.

C. J. (M) *Ulcerative colitis (clinical diagnosis tubercle of bowel).*

8/ 5/6	0.8	
19/ 5/6		TR. $\frac{1}{1000}$
2/ 6/6		TR. $\frac{1}{1000}$
5/ 6/6	0.8	TR. $\frac{1}{500}$
12/ 6/6	1.7	
19/ 6/6	1.3	
4/ 7/6	0.9	
20/ 7/6	1.3	
23/ 7/6		TR. $\frac{1}{1000}$
24/ 7/6	0.9	
31/ 7/6	1.6	
4/ 8/6		TR. $\frac{1}{1000}$
7/ 8/6	0.6	
16/ 8/6		TR. $\frac{1}{500}$
27/ 8/6	0.8	
7/ 9/6		TR. $\frac{1}{500}$
10/ 9/6	1.1	
28/ 9/6	1.0	
8/10/6	1.2	
20/12/6	1.7	
24/ 1/7	Died.	

M. G. *Lumbar and double psoas abscess.*

7/ 3/6	2.0
22/ 3/6	1.5
20/ 4/6	0.78
21/ 5/6	1.3
9/ 5/6	0.7
21/ 6/6	0.6
29/ 6/6	Died.

A. C. (F) *Hæmoptysis.*

16/ 3/6	1.0
22/ 3/6	1.4

H. C. (M) *Tubercle of peritoneum.*

18/ 7/6	1.1	
21/ 7/6	1.3	
24/ 7/6		TR. $\frac{1}{500}$
25/ 7/6	0.7	
1/ 8/6	0.7	
2/ 8/6		TR. $\frac{1}{500}$
3/ 8/6	2.4	
28/ 8/6	1.0	Discharged 19/9/6; died, 1907.

A. B. (M) *Hip disease.*

18/ 9/6	1.0	
19/ 9/6	1.0	Discharged.
28/ 9/6	0.8	

A. W. (F) *General tuberculosis and tuberculosis of peritoneum.*

5/ 6/6 0.8
7/ 6/6 1.2 17
8/ 6/6 TR $\frac{1}{1000}$
12/ 6/6 1.6
19/ 6/6 1.0
20/ 6/6 TR. $\frac{1}{1000}$ Died.

M. (M) *Tubercle of Pleura.*

9/ 4/7 0.3
22/ 4/7 1.0
1/ 5/7 1.2
3/ 5/7 TR. $\frac{1}{2500}$
17/ 5/7 0.6
18/ 5/7 TR. $\frac{1}{2500}$ Discharged improved, 12/6/7.

F. L. 28 (M) *Tubercle of hip, amputation of thigh.*

25/ 6/6 1.2
24/ 7/6 1.3
31/ 7/6 1.7
4/ 8/6 TR. $\frac{1}{1000}$
7/ 8/6 0.8
27/ 8/6 0.6 Died 19/9/6.

C. L. (M) *Tubercle of Knee—Amputation of leg.*

30/ 4/6 0.7
8/ 5/6 0.8

G. H. (M) *Tubercle of peritoneum.*

5/ 2/6 0.78
26/ 7/6 1.2
3/ 8/6 1.9
28/ 8/6 0.8 Discharged improved 4/9/6.

J. W. 22 years (M) *Tuberculosis urinary tract.*

26/ 3/6 0.03 ? TB in urine.
10/ 4/6 0.75 TR. 3 hours previously.
14/ 4/6 0.85
17/ 4/6 3.0 TR. 23 hours previously.
23/ 4/6 0.8 TR. 5 hours previously.
30/ 4/6 0.3
2/ 5/6 1.3
7/ 5/6 0.9
8/ 5/6 0.8
14/ 5/6 2.0
15/ 5/6 1.0
21/ 5/6 1.9
22/ 5/6 1.3
28/ 5/6 1.5
29/ 5/6 TR. $\frac{1}{500}$ mgm.
30/ 5/6 0.9
4/ 6/6 0.9
5/ 6/6 TR $\frac{1}{500}$ mgm.
7/ 6/6 1.5
12/ 6/6 1.4 TR. $\frac{1}{1000}$ mgm.
15/ 6/6 1.4
18/ 6/6 1.8
19/ 6/6 TR. $\frac{1}{500}$ mgm.
20/ 6/6 0.9
21/ 6/6 TR. $\frac{1}{500}$ mgm.
25/ 6/6 0.8
26/ 6/6 TR $\frac{1}{500}$ mgm.
27/ 6/6 1.1
3/ 7/6 0.7

4/ 7/6		TR $\frac{1}{500}$ mgm.	
9/ 7/6	1.0		
11/ 7/6		TR $\frac{1}{500}$ mgm.	
17/ 7/6	0.7	TR $\frac{1}{500}$ mgm.	
23/ 7/6	1.8		
24/ 7/6		TR $\frac{1}{500}$ mgm.	
30/ 7/6	1.2		
31/ 7/6	2.4	TR $\frac{1}{500}$ mgm.	
6/ 8/6	1.0		
7/ 8/6		TR $\frac{1}{500}$ mgm.	
24/ 8/6	0.7	TR $\frac{1}{1000}$ mgm.	
6/ 9/6	0.7		
11/ 9/6	1.1		
13/ 8/7		No TB. in urine.	Improved.

E. T. 31 years (?) (F) *Addison's disease.*

29/10/5	0.7		
27/11/5	0.7		
19/12/5	0.6		
31/ 9/6	1.0		
1/ 5/6	1.0		

J. S. (M) *Psoas abscess.*

10/11/5	0.4	15/11/5	0.4

S. (M) *Tuberculosis of lungs and intestine.*

28-11-6	1-5		

A. S. (M) *Tuberculosis pulmonalis.*

4/ 4/7	0.6		
6/ 4/7	0.6	TR $\frac{1}{2000}$	
22/ 4/7	0.9		
25/ 4/7		TR $\frac{1}{2000}$	
2/ 5/7	1.3		
3/ 5/7		TR $\frac{1}{2000}$ mgm.	
17/ 5/7	1.1		
18/ 5/7		TR $\frac{1}{1000}$ mgm.	
1/ 6/7	0.8		

Death—*Tubercle of lungs, pleura and spleen.*

—. R. (M) *Tubercle peritoneum.*

20/ 6/7	0.7		
10/ 7/7	0.6		
31/ 7/7	1.0		
14/ 8/7	1.0		Tubercule TR.
27/ 8/7	0.9		Under treatment.

M. R. (19) *Tubercle of hip.*

13/ 5/7	0.8		
1/ 7/7		TR $\frac{1}{2000}$ mgm.	
13/ 7/7	0.9		
24/ 7/7		TR $\frac{1}{2000}$	
24/ 8/7	1.0		
26/ 8/7		TR $\frac{1}{2000}$	Under observation.

J. N. (M) ? *Addison's.*

8/10/6	0.8		
17/10/6	0.9		
20/11/6	1.3		Death: *Phthisis, tubercle of Peritoneum, Thrombosis of mesenteric vessels with gangrene of bowel, peritonitis.*

E. N. (F) *Lupus of Nose.*

11/7/7	0.9		

A. M. (F) *Tuberculous cystitis.*

21/ 9/6 1.2
28/ 9/6 1.2
5/11/6 1.6

V. M. (32) *Tuberculous epididymitis, operation*

28/ 7/6 1.2
1/ 8/6 0.6
3/ 8/6 1.8
4/ 8/6 TR $\frac{1}{1000}$
31/ 8/6 1.5
3/ 9/6 1.7 TR $\frac{1}{2000}$
4/ 9/6 1.0
10/ 9/6 1.1
14/ 9/6 TR $\frac{1}{1000}$
17/ 9/6 1.6
18/10/6 1.4
19/10/6 1.0 (TR $\frac{1}{1000}$ previously)
18/12/6 0.8
19/12/6 0.8 TR $\frac{1}{2000}$
23/ 1/7 1.0
26/ 1/7 TR $\frac{1}{1000}$
9/ 2/7 1.0
16/ 2/7 TR $\frac{1}{5000}$
9/ 3/7 1.0
2/ 4/7 0.8
4/ 4/7 TR $\frac{1}{5000}$
24/ 4/7 1.1 Tuberculous sinus healed.

F. M. (?) *General miliary tuberculosis, peritoneum, viscera and thymus affected.*

9/ 1/6 0.4
10/ 1/6 0.4
23/ 1/6 1.3
7/ 2/6 0.8 Died.

A. M. (F) *Lupus.*

23/ 1/6 1.0

(In private practice) (*Tubercle of Lymph glands, etc.*)

Miss C.

1/ 7/7 1.4
6/ 7/7 1.2

Mme. H.

12/ 6/7 0.75
28/ 8/7 1.0

Mme. L.

30/ 1/7 0.7

Miss B.

11/12/6 1.0

Mme. C.

11/12/6 1.6
30/ 1/7 0.8

Miss D.

30/ 4/6 0.8
20/ 6/6 0.9

Mme. X.

29/ 5/6 1.2
12/ 6/6 1.1
10/ 7/6 1.0
6/ 8/6 0.5
29/ 8/6 0.8
18/12/6 0.75
7/ 5/7 0.8

Mme. C.

20/ 6/6 0.6
4/ 7/6 1.0

16/ 7/6 0.9
29/ 8/6 0.7
31/10/6 1.2
11/12/6 1.4
30/ 1/7 1.3

Mme. K.
7/ 5/6 0.6

Miss F. (Tuberculous glands of neck). (T.R. every 14 days, about).
20/12/6 1.0
14/ 1/7 1.3
8/ 2/7 1.2
12/ 3/7 0.6
15/ 3/7 1.5
27/ 3/7 0.9

Miss T. Tubercle of spine.
7/ 4/7 0.8
20/ 6/7 0.35
29/ 6/7 1.2
27/ 3/6 0.28

Girl (?) Tubercle.
23/ 7/6 0.5
21/ 8/6 0.8

Miss H. *Tubercle of pelvis.*
5/ 9/6 1.3
19/10/6 1.2

Mr. de W.
22/10/6 1.2 Tuberculin administered; no improvement.
29/10/6 1.1
16/ 7/7 1.0
27/ 8/7 0.7

Mr. J.
30/ 7/7 1.2
1/ 8/7 1.0

J. B.
23/ 7/7 0.8
26/ 7/7 1.3

STAPHYLOCOCCUS.

S. McD. (F) 50. *Pernicious Anæmia.*
17/ 6/7 1.0
24/ 6/7 0.9
4/ 7/7 1.5
19/ 7/7 1.1

T. A. M. (M) 8. *Empyema.*
15/ 5/7 1.0
3/ 6/7 0.9
17/ 6/7 1.0

H. M. (M) 41. *Septic arm.*
23/ 3/7 1.5

A. M. (55). *Mycosis Fungoides.*
8/ 4/7 1.3
9/ 4/7 1.1 (cocci)
1.1 (B.K.S. cocci)

M. G. (F) *Abscess of Thigh.*
11/ 6/7 1.0
24/ 6/7 0.9

C. V. (F) *Pulmonary tubercle septicæmia Parotitis* (*death*).

14/ 5/6 0.6
18/ 5/6 Staphylococci 340 mill.

C. R. (M) *Gangrene of Lung.*

30/ 6/6 1.3
10/ 7/6 Vaccine 300 mill.

W. P. (49) (M) *Pernicious anæmia* (death).

11/ 3/7 1.1
22/ 3/7 1.1

A. B. (19) (M) *Pyopneumothorax, sepsis.*

22/ 1/7 1.2
24/ 1/7 1.3
V. Staphylococci 250 mill.

W. C. (30) (M) *Tubercle of femur and staphylococcal infection.*

3/ 4/6 0.6
11/ 4/6 0.49
2/ 5/6 0.5

B. Kent (20) (M) *Necrosis of femur, amputation.*

8/ 4/7 0.7
9/ 4/7 0.8
10/ 4/7 1.1
16/ 4/7 v. staphylococci.
22/ 4/7 0.8
24/ 4/7 1.0
29/ 4/7 1.1
30/ 4/7 1.1
7/ 5/7 0.7
8/ 5/7 0.7 *In statu quo.*
24/ 5/7 1.1
7/ 6/7 0.9

E. C. *Acute rheumatism.*

22/ 1/7 1.3
24/ 1/7 1.3

E. W. (F) *Empyema.*

26/ 8/7 1.0 Still under treatment.

Mrs. T——r *Empyema.*

10/ 7/7 0.65 500. 1000, 2000 mill, vaccine administered.

Mrs. T——g *Empyema.*

15/ 4/7 1.5
22/ 4/7 0.76
29/ 1.4
29/ 5/7 1.0
29/ 6/7 1.6
18/ 7/7 1.5
10/ 8/7 1.2
1000. mill (2)
2500. mill (2)

Mrs. F. *Septicæmia.*

22/ 3/7 0.47
28/ 3/7 0.8
3/ 4/7 0.9 300. mill: staphylo (2) recovered.

Mr. T——y. (?)

10/ 5/6 0.7

Mrs. R. B. *Neoformans, carcinoma mammæ.*

15/11/6 1.0
29/11/6 1.2 Vaccine administered—no improvement.

M. G. (F) *Lumbar abscess.*

16/ 5/6 0.8
21/ 5/6 0.8
9/ 6/6 0.8

S. (M) *Empyema.*

18/ 4/7 0.5
29/ 4/7 1.3
4/ 5/7 v. 300 mill. staphylococci
7/ 5/7 0.7
21/ 5/7 1.1 v. 300 mill. staphylococci
3/ 6/7 0.9

B. DIPHTHEROID.

P. S. (M) *Tuberculous hip, saprœmia.*

23/ 5/7 1.4
25/ 5/7
27/ 5/7 1.2

—. S. (M) *Empyema.*

28/ 6/7 1.3

B. COLI.

C. R. (30) *Gangrene of lungs.*

18/ 7/6 1.3
23/ 7/6 1.0
27/ 7/6 1.3
3/ 8/6 v. 90 mill. coli.

W. T. (M) *Pernicious Anæmia.*

1/ 5/7 0.6
12/ 5/7 V.B. Coli 200 mill.
17/ 5/7 V.B. Coli 200 mill.

Miss D. (17) *Bacilluria* (Colon).

9/ 6/6 1.3

Miss H. *Peritonitis.*

17/ 12/6 0.8
1.0
28/12/6 v. 200 mill.

STREPTOCOCCI.

C. R. (M) *Abscess of lung.*

10/ 7/6 1.0

W. A. W. (M) *Leukanæmia.*

9/ 7/7 1.3

W. T. (M) *Pernicious Anæmia* (39 years).

1/7 1.8
23/1/7 0.6
2/2/7 0.8
6/2/7 1.2
18/2/7 0.8
27/2/7 0.6
2/3/7 0.7

—. Smith (M). *Empyema.*
13/ 4/7 1.0
16/ 4/7 v. 300 mill.
26/ 4/7 1.0
15/ 5/7 v. 300 mill.

S. (M) *Pernicious Anæmia.*
15/ 6/7 1.0
20/ 6/7 v. 300 mill.
26/ 6/7 1.0

A. S. (M). *Pulmonary tubercle and sepsis.*
22/ 5/7
3/ 6/7 0.8 v. 300 mill.

C. (23). *Varicocele, sepsis* (death).
v. 300 million streptococci.

Mrs. F. (30). *Septicæmia.*
14/ 3/7 0.7 v. strepto 12/3/7
3/7 0.5

Miss L. *Septic bronchitis.*
16/ 5/7 0.6

PNEUMOCOCCUS.

Mc.D. (F) 50 years. *Pernicious Anæmia.*
24/ 6/7 1.4

H. *Empyema.*
5/ 6/7 1.6

PYOCYANEUS.

W. T. (M). *Pyæmia after amputation.*
15/ 6/6 0.9
20/ 6/6 0.8
7/ 7/6 v = 200 mill.
10/ 7/6 0.6
18/ 7/6 1.0 Discharged 7/6/7.

F. L. (M) 29. *Tubercle of hip and lungs—amputation—sepsis, death.*
15/ 6/6 1.1
20/ 6/6 0.9
5/ 7/6 v. 205 millions.
10/ 7/6 1.6
18/ 7/6 1.3

TYPHOID.

—. K. (M). *Enteric* (20 years).
19/ 4/7 1.6

E. B. *Enteric.*
9/ 4/6 0.52
1.0

E. T. *Acute periostitis.*
5/ 6/7 1.1
17/ 6/7 1.0
Discharged 19/6/7